UNITED STATE EPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/254,288	04/02/99	TESCHNER	W 040433/0177

HM22/0612

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EXAMINER	
SAUCIER,S	
ART UNIT	PAPER NUMBER
1651	5

DATE MAILED: 06/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/254,288	Teschner et al.
Examiner	**Group Art Unit**
Sandra Sauci r	1651

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *14-34* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *14-34* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 14-34 are pending and are considered on the merits.

Specification

The disclosure is objected to because of the following informalities: It lacks the proper headers such as "Description of the Prior Art, Summary of the Invention, Detailed Description of the Invention, etc..

Page 11 , zinc is misspelled.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 14-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Citrate is a dicarboxylate having 4 carbons. It is unclear how the exchange of citrate for a dicarboxylate which may be citrate (because the term "dicarboxylate" encompasses citrate) creates a medicament which does not take up metals as the preamble of claim 14 states. Claims 14 and 16 are, therefore, confusing.

Claim 14 is also indefinite because the term "water soluble mono or dicarboxylate" is overlapping with the term "organic mono or dicarboxylate". A compound which contains a carboxy radical (mono-carboxylate for example) is by definition an organic compound. See Grant and Hackh's Chemical Dictionary, page 412. It is suggested that "an organic mono or dicarboxylic acid" be canceled.

Claims 14 and 31 recite "undesired metals". This is not a definite term, but changes with the desire of the practioner. Thus, the metes and bounds of the claim are not definite.

Claim 15 should have "forth" instead of "for".

Claim 16 is indefinite because "an organic carboxylic acid" may be a

mono-, di- or tri-acid. The term expands the independent claim which is limited to mono and di-carboxylic acids.

Please note that the claims vary in their usage of "carboxylate" and "salt of carboxylic acid". It is suggested that applicants chose "salts or carboxylic acids" and use it consistently.

Claim 20 recites "from salts" in the last line. What salts are meant? The citrate salts, the tartrate salts, metal salts etc. The step of separating is not in active language, thus, it may not occur.

Claim 34 has new matter, but this is considered to be merely a typographical error instead of intentional insertion. Please correct "200µg/l" to read 200ηg/l as in the original claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States, (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 14-17, 19-23, 26, 28, 31-34 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by US 5561115 [A].

The claims are directed to a plasma protein containing product which is substantially free from undesired metals.

US 5561115 discloses a process of preparing an albumin solution comprising adding sodium caprylate to Cohn fractions II+III of plasma. As Cohn fractions are routinely produced from plasma derived from citrated blood, they are considered to contain at least some of the original citrate. The sodium caprylate is said to separate the colloidal solution into a supernatant phase and a disperse or colloidal phase (col. 3, l. 3). Please note that this is not a

precipitating condition. A colloid is not a precipitate, and therefore by definition, the conditions are non-precipitating see Grant and Hackh's Dictionary, page 145. The addition of sodium caprylate while heating also inactivates viruses (col. 5, l. 3). The suspension is then further diafiltered with 0.02M sodium caprylate and treated by filtration to prepare a sterile albumin preparation (col. 3 and example I).

US 5561115 discloses albumin containing 7.53 ppb aluminum (col. 7, Results).

Claims 14-16, 18-23, 28, 29, 31-34 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 5372997 [B].

US 5372997 discloses a process for removing aluminum from albumin comprising:

adding acetic acid (acetate) to the Cohn's fraction V, adding NaOH to the fraction, running the solution through an anion exchange column which has been washed with NaCl and equilibrated with NaAc. Because only the presence of NaCl is required in claim 29, it is considered to be reasonably expected that an exchange column which has been washed with NaCl will have at least some NaCl remaining on it, and this fulfills the claim limitation. Because the Cohn's process for fractionating plasma has a step of adding EtOH at a low temperature, which is known to inactivate viruses, a viral inactivation is considered to have been performed on the albumin prior to the exchange of citrate. A low aluminum product is produced and stored in low aluminum containing glass.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the

contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-29, 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5561115 [A] or US 5372997 [B] and US 5118794 [C].

The claims are directed to a process for reducing the concentration of metals in citrated plasma or a citrated plasma product comprising:
exchanging, particularly by filtration or a chromatographic method, the citrate anion for a mono- or di-carboxylic anion, particularly tartrate or caprylate anions, without precipitating the plasma proteins,
recovering a plasma protein,
carrying on. Some of the claims require a virus inactivation step after removal of the citrate-bound metal.

The references are relied upon as explained below.

US 5561115 discloses a process of preparing an albumin solution comprising adding sodium caprylate to Cohn fractions of plasma. As Cohn fractions are routinely produced from plasma derived from citrated blood, they are considered to contain at least some of the original citrate. The sodium caprylate is said to separate the colloidal solution into a supernatant phase and a disperse or colloidal phase (col. 3, l. 3). Please note that this is not a precipitating condition. A colloid is not a precipitate, see Grant and Hackh's Dictionary, page 145. The suspension is then further diafiltered with 0.02M sodium caprylate and treated by filtration to prepare a sterile albumin preparation (col. 3 and example I). This gives a preparation with low aluminum and citrate content. This reference lacks the specific disclosure of a step for the inactivation of viruses performed after recovery of the processed albumin.

US 5118794 discloses that viral inactivation in albumin may be performed by terminal heat treatment.

The addition of the terminal step of treating the albumin to inactivate viruses by heating to the method as disclosed by the primary references of US 5561115 or US 5372997 would have been obvious when the primary

references were taken with the method shown by US 5118794 which demonstrates terminal pasteurization of albumin.

Claims 14-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5229498 [E] in combination with US 5372997 [B].

The references are relied upon as described below.

US 5229498 discloses a method of removing multivalent metal cations, in particular, aluminum from a protein solution by exchange with monovalent metal cations such as sodium or potassium cations by gel or dia-filtration.

Albumin is an exemplified protein. 1M sodium chloride is added to the albumin and the resulting albumin solution was diafiltered against 1M NaCl. The concentration of multivalent metal cations is reduced to below 30µg/l (example 1). In example 4, terminal heat treatment is demonstrated. In example I, a Cohn fraction is used. A Cohn fraction is produced by adding EtOH which is known to inactivate viruses.

US 5372997 discloses the use of a low aluminum containing glass to store albumin which has a reduced aluminum content (col. 6).

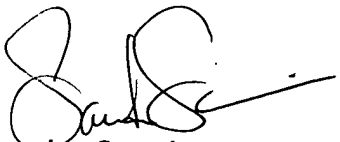
The substitution of sodium caprylate or sodium tartrate or sodium acetate for the sodium chloride in the method of US 5229498 would have been obvious because '498 teaches a non-limited exchange of monovalent metal cations for multivalent metal cations, in particular the exchange of sodium cation for aluminum cation. It is apparent that sodium caprylate, sodium acetate or sodium tartrate are sodium salts and therefore release a sodium cation in solution. Therefore, sodium tartrate, sodium acetate, etc., may be substituted for the exemplified sodium salt, sodium chloride in accordance with the teachings of '498.

The subsequent storage of the processed albumin in low aluminum-containing glass would have been obvious when the primary reference was taken with the disclosure of US 5372997 which shows that albumin solutions which have had the undesired metal cations removed, will not pick up more metal cations if stored in a low metal-containing container.

One of skill in the art would have been motivated at the time of invention to make these substitutions in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Service Desk at (703) 308-0196. The number of the Fax Center for the faxing of papers is (703) 308-4227.



Sandra Saucier
Primary Examiner
Art Unit 1651
June 9, 2000